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Sleep apnea reduces the amount of computational deep sleep in the right frontopolar area in school-aged children

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HIGHLIGHTS

- Obstructive sleep apnea results in local NREM sleep depth differences.
- Right frontopolar area seems to be vulnerable in children's obstructive sleep apnea.
- Local deep sleep differences may account for the different daytime symptoms found in children's obstructive sleep apnea.

ABSTRACT

Objective: Obstructive sleep apnea (OSA) causes different symptoms in children, even though polysomnographic parameters that assess sleep quality may remain normal. Our spectral analysis of NREM sleep revealed local deep sleep reductions in adult OSA patients. We hypothesize that our method would also reveal local changes in pediatric OSA patients.
Methods: Polysomnographies were part of a larger study evaluating snoring in school-aged children. All right-handed children with OSA with matched peers (n = 10 + 10) were included. The median sleep depth (in Hz) and the amount of deep sleep <4 Hz (DS%) were extracted for the whole NREM sleep time and for the first four NREM sleep episodes from frontopolar, central and occipital EEG-channels.
Results: The main findings were that NREM sleep was lighter and DS% decreased in the right frontopolar area (p-values 0.034 and 0.019) in the OSA group when compared with the control group.
Conclusion: Local sleep quality changes might provide new insights to evaluate the effects of pediatric OSA as our method revealed a local computational deep sleep decrease in the right frontopolar area in the OSA group.
Significance: The presented findings might implicate delayed local cortical development in children's OSA, which may account for the cognitive problems found in pediatric OSA.

1. Introduction

It has been estimated that obstructive sleep apnea (OSA) affects 1–3% of children (Ali et al., 1993; Bixler et al., 2009; Gislason and Benediktsdóttir, 1995). Children's OSA is known to cause different symptoms that include deficits in cognitive performance (Friedman et al., 2003; Halbower et al., 2006), inattention leading to poor school performance (Gozal, 1998) and behavioral problems such as hyperactivity (Guilleminault et al., 1981; Melendres et al., 2004; O'Brien et al., 2003). Despite the remarkable daytime symptoms among pediatric OSA patients, they may preserve the normal sleep stage distribution with no sleep fragmentation (Goh et al., 2000; Yang et al., 2010). It has been suggested that among children the enhanced sleep pressure induced by OSA would be strong enough to preserve the sleep quality (Yang et al., 2010) and that the cause behind the symptoms is to be found elsewhere.

The In adults, one of the leading characteristics of self-reported good quality sleep seems to be the amount of SWS or automatically extracted slow wave activity (SWA) (Keklund and Åkerstedt, 1997; Åkerstedt et al., 1997; Westerlund et al., 2014). SWS and SWA are

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most often found during deep sleep (stage N3). They are considered as markers of sleep quality and sleep depth playing an important role in the regulation of sleep (Tononi and Cirelli, 2003; Borbély and Achermann, 1999). In addition, local activation of certain brain areas during wakefulness is found to induce local increase in SWA in the subsequent night in that particular brain area (Kattler et al., 1994; Murphy et al., 2011; Huber et al., 2004; Pugin et al., 2015). In children, SWA can also be considered to express the synaptic density and development of neural plasticity (Kurth et al., 2010a, 2012; Campbell et al., 2011; Campbell and Feinberg, 2009). The occipital areas in children normally develop first and frontal areas last (Shaw et al., 2008), and an increased amount of deep sleep can be found in the brain regions that are undergoing the maturating process (Kurth et al., 2012). This might reflect the importance of deep sleep in school-aged children in the brain maturing processes.

We have used computational sleep depth analysis of NREM sleep in adult OSA patients and found significant differences in the amount of deep sleep between OSA patients and control subjects (Saunamäki et al., 2009). In OSA, computational deep sleep was diminished frontopolarly, centrally and occipitally in both hemispheres. Continuous positive airway pressure (CPAP) treatment abolished some of the differences, but patients with OSA continued to present a reduced amount of deep sleep in the right frontopolar area. In addition, OSA patients showed deficits in visuoconstructive tasks reflecting deficits in the function of the right hemisphere.

To the best of our knowledge, the effects of OSA on local sleep EEG differences in school-aged children have not been previously studied. In this study, we compare the local NREM sleep depth differences of 10 OSA children to the values of 10 age and sex-matched control subjects. We believe that, as in adults, changes in the computational sleep depth parameters will be observed among children with OSA even if the effect of OSA on conventional sleep parameters is minor.

2. Methods

The present study is a part of a larger cross-sectional study designed to assess sleep-related breathing disorders in Finnish school-aged children. The parents of children in the first or third grade in 32 randomly selected schools in Tampere, Finland were given the Finnish version of the Sleep Disturbance Scale for Children (SDSC) (Bruni et al., 1996). In total, 1538 questionnaires were delivered and 329 were returned. The SDSC is a questionnaire that assesses the frequency of sleep problems. The questionnaire contains statements scored on a five-point scale: 1 = never, 2 = occasionally (1–2 nights a month), 3 = sometimes (1–2 nights a week), 4 = often (3–5 nights a week), and 5 = always (every night).

The questionnaire included a question about snoring: "How often does your child snore?". In total, 33 children had SCSD scores 4 or 5 (snoring at least 3–5 nights a week), and 259 children had SCSD scores 1 or 2 (non-snorers). All 33 snoring children and an equal number of sex and age-matched non-snoring children were asked to participate in a polysomnography (PSG) study comprising two nights in-hospital polysomnography. Altogether, 27 snoring children agreed to participate in the PSG study. In addition, 36 non-snoring children were studied. The Ethical Committee of Pirkanmaa Hospital District and the City of Tampere approved the study. Written informed consent to participate in the study was obtained from the parents of all the children.

2.1. Recordings and visual analysis

The polysomnography comprised six EEG derivations (Fp1-A2, Fp2-A1, C3-A2, C4-A1, O1-A2 and O2-A1), two electrooculography (EOG) channels, submental muscle tonus, electrocardiogram, airflow by nasal pressure transducer and thermistor, thoracoabdominal respiratory movements, electromyography from the abdomen and diaphragm, blood oxygen saturation with pulseoximetry, transcutaneous carbon dioxide tension, leg movements, body position and sleep mattress signal. Polysomnographies were recorded with an Embla N7000 device (Embla®, Natus Medical Inc., USA). The EEG signals were sampled at 200 Hz (16 bits) with a bandwidth of 0.3–90 Hz.

The first night served as an adaptation night, and the second night was used in the statistical analyses. As the project was started before the revision of the sleep staging rules, the frontopolar EEG-channels Fp1 and Fp2 were used instead of the frontal channels F3 and F4 that are recommended nowadays. The sleep staging was, however performed in accordance with the rules established by the AASM in 2007 (Iber et al., 2007), with the exception of the EEG-channel. The recordings were classified into the sleep stages by two independent clinical neurophysiologists. A senior neurophysiologist performed the consensus sleep stage scoring by evaluating the differences between the scorings. The level of agreement between the two independent scorers was 85.8% (Kappa = 0.76).

The apnea–hypopnea index (AHI) was calculated as the number of obstructive apneas and hypopneas per hour of sleep using the rules of the AASM 2012 (Berry et al., 2012). Obstructive apneas were defined as at least 90% reduction in the thermal signal amplitude lasting at least two breaths with continuous respiratory effort. Hypopneas were defined as diminution of at least 30% of the nasal pressure amplitude (lasting at least 2 breaths) with a simultaneous cortical arousal or desaturation of $\geqslant$3%. Microarousals were scored according to the criteria of the American Sleep Disorders Association (1992). Sleep cycles were defined according to the criteria of Feinberg and Floyd (1979). In children, the first REM episode is sometimes missing, so we decided to adopt the rule presented by Jenni and Carskadon (2004) and divided the first NREM episode into two if deep sleep was interrupted by wakefulness or lower sleep stages for more than 12 min.

Fourteen out of 27 snoring children had at least mild sleep apnea (obstructive AHI, OAHI >1/h, OSA). Four of these children were left-handed and had to be omitted from the present study that evaluated local EEG differences. As a result, the final OSA-group comprised ten children (4 boys, 6 girls). A child neurologist determined the Tanner stage of the children in order to measure their pubertal status; two boys and two girls with OSA presented Tanner stage 2, and the others were in stage 1 (Tanner, 1962). The control group was formed from the non-snoring group. The requirements for the control peers were 1: same sex, 2: right-handedness, 3: same Tanner puberty score, 4: AHI < 1/h, 5: age. Matching peers were found for each child with OSA.

All children included in the study had 4 sleep cycles (and NREM episodes), but only five OSA children and seven control children had 5 NREM episodes. Therefore, the NREM episode comparisons were limited to the first four episodes (NREM1–4).

2.2. Spectral sleep EEG analysis

The mean frequency values were computed from each of the six EEG channels by applying the method described in detail previously (Huupponen et al., 2004, 2005). Mathematically, determination of the mean frequency was formulated in the following way. Let $S(f) = X(f) + jY(f)$ be the complex spectrum estimate of an EEG epoch of L samples and let $w = \{w[n]\}$, $0 \leqslant n \leqslant L-1$ be a discrete window function of length L. The corresponding amplitude spectrum value $A(f)$ at frequency f can then be computed as follows:

$$A(f) = \frac{2\sqrt{X^2(f) + Y^2(f)}}{\sum_{n=0}^{L-1} w[n]}$$